Cardiorespiratory arrest in children (out of hospital)

Search date November 2014

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ABSTRACT

INTRODUCTION: Cardiorespiratory arrest outside hospital occurs in approximately 1/10,000 children per year in resource-rich countries, with two-thirds of arrests occurring in children under 18 months of age. Approximately 45% of cases have undetermined causes, including sudden infant death syndrome. Of the rest, 20% are caused by trauma, 10% by chronic disease, and 6% by pneumonia. METHODS AND OUTCOMES: We conducted a systematic overview, aiming to answer the following clinical question: What are the effects of treatments for non-submersion out-of-hospital cardiorespiratory arrest in children? We searched: Medline, Embase, The Cochrane Library, and other important databases up to November 2014 (BMJ Clinical Evidence overviews are updated periodically; please check our website for the most up-to-date version of this overview). RESULTS: At this update, searching of electronic databases retrieved 192 studies. After deduplication and removal of conference abstracts, 81 records were screened for inclusion in the overview. Appraisal of titles and abstracts led to the exclusion of 68 studies and the further review of 13 full publications. Of the 13 full articles evaluated, three systematic reviews were added at this update. We have also added eight studies to the Comment section. We performed a GRADE evaluation for three PICO combinations. CONCLUSIONS: In this systematic overview, we categorised the efficacy for nine interventions based on information about the effectiveness and safety of airway management and ventilation (bag-mask ventilation and intubation), bystander cardiopulmonary resuscitation, direct-current cardiac shock, high dose and standard dose intravenous adrenaline (epinephrine), intravenous sodium bicarbonate, intubation versus bag-mask ventilation, targeted temperature management, and training parents to perform resuscitation.

QUESTIONS

INTERVENTIONS

TREATMENTS FOR NON-SUBMERSION OUT-OF-HOSPITAL CARDIORESPIRATORY ARREST IN CHILDREN

Footnote

*Although we found no direct evidence to support their use, widespread consensus holds that, on the basis of indirect evidence and extrapolation from adult data, these interventions should be universally applied to children who have arrested.

Key points

- Cardiorespiratory arrest outside hospital occurs in approximately 1/10,000 children per year in resource-rich countries, with two-thirds of arrests occurring in children under 18 months of age.

  Approximately 45% of cases have undetermined causes, including sudden infant death syndrome. Of the rest, 20% are caused by trauma, 10% by chronic disease, and 6% by pneumonia.

- Overall survival for out-of-hospital cardiorespiratory arrest in children is poor.

  Overall survival for children who sustain cardiorespiratory arrest outside hospital not caused by submersion in water is about 4%.

  Of those who survive, between half and three-quarters will have moderate to severe neurological sequelae.

- There is very poor evidence for any intervention in cardiorespiratory arrest in children. Despite this, placebo-controlled trials for most accepted interventions would be ethically challenging in this population.

- High-quality chest compressions with minimal interruption and immediate airway management and ventilation are widely accepted to be key interventions.

  On the basis of observational evidence and experience, most clinicians regard bystander cardiopulmonary resuscitation to be an important intervention in out-of-hospital cardiopulmonary arrest, although the effects of training parents in cardiopulmonary resuscitation are unknown.

- Ventilation with a bag and mask seems as effective as intubation. The most suitable method for the situation should be used.

- Direct current cardiac shock is likely to be beneficial in children with ventricular fibrillation or pulseless ventricular tachycardia.

Ventricular fibrillation or pulseless ventricular tachycardia are the underlying rhythms in 10% of cardiorespiratory arrests in children, and are associated with a better prognosis than asystole or pulseless electrical activity.

Defibrillation within 10 minutes of the arrest may improve the outcome.

- Intravenous adrenaline is widely accepted to be the initial medication of choice in a paediatric cardiac arrest.

  The standard dose of intravenous adrenaline is 0.01 mg/kg.

  We don't know how high-dose adrenaline (0.1 mg/kg) and standard-dose adrenaline compare in children with cardiac arrest. The evidence is sparse and should be interpreted with caution. The AHA does not recommend use of high-dose adrenaline.

  We found no direct information from RCTs about the effects of intravenous sodium bicarbonate in children who have arrested in the community.

- The effects of cooling a child after arrest are unknown.

Clinical context

GENERAL BACKGROUND

Out-of-hospital cardiorespiratory arrest in children, although rare, is associated with low survival rates and poor functional neurological outcomes in children who survive.

FOCUS OF THE REVIEW

This overview aims to determine the evidence available to support the use of widely practised and taught interventions such as Paediatric Advanced Life Support measures in the management of out-of-hospital cardiorespiratory arrest in children. These include airway management and ventilation, bystander cardiopulmonary resuscitation, direct current cardiac shock, standard-dose intravenous adrenaline, and induced hypothermia. Evidence for the use of high-dose intravenous adrenaline and intravenous sodium bicarbonate has also been reviewed. These interventions are not currently recognised to be standard practice, but have been widely used in the past. Training programmes for parents to perform cardiopulmonary resuscitation exist widely and are popularly recommended; as such, this intervention has also been included in this overview.

COMMENTS ON EVIDENCE

Very few clinical trials have been conducted to evaluate the effectiveness of therapies for out-of-hospital cardiorespiratory arrest in children. Despite the lack of evidence, placebo-controlled trials for most accepted interventions would be ethically challenging in this population. Because of the paucity of RCT evidence, some data from observational studies have also been included in the Comment sections of this overview.

SEARCH AND APPRAISAL SUMMARY

The update literature search for this overview was carried out from the date of the last search, December 2009, to November 2014. For more information on the electronic databases searched and criteria applied during assessment of studies for potential relevance to the overview, please see the Methods section. Searching of electronic databases retrieved 192 studies. After deduplication and removal of conference abstracts, 81 records were screened for inclusion in the overview. Appraisal of titles and abstracts led to the exclusion of 68 studies and the further review of 13 full publications. Of the 13 full articles evaluated, three systematic reviews were added at this update. Based upon their own search, the contributors added eight studies to the Comment sections.

ADDITIONAL INFORMATION

Although out-of-hospital cardiorespiratory arrest in children is associated with low survival rates, high-quality chest compressions with minimal interruption, immediate airway management, and ventilation are widely accepted to be key interventions. Ventilation with a bag and mask seems as effective as intubation. The most suitable method for the situation should be used. Direct-current cardiac shock is likely to be beneficial in children with ventricular fibrillation or pulseless ventricular tachycardia. These are the underlying rhythms present in 10% of cardiorespiratory arrests in children, and are associated with a better prognosis than asystole or pulseless electrical activity. Defibrillation within 10 minutes of the arrest may improve the outcome. Evidence from observational studies suggests that standard-dose intravenous adrenaline and bystander cardiopulmonary resuscitation are likely to be beneficial.

DEFINITION

This overview covers non-submersion, out-of-hospital cardiorespiratory arrest in children. The paediatric Utstein style definition [1] is cessation of cardiac mechanical activity, determined by the inability to palpate a central pulse, unresponsiveness, and apnoea occurring outside of a medical facility and not caused by submersion in water. The use of pulse palpation in the determination of cardiorespiratory arrest has been de-emphasised in the Advanced Life Support guidelines due to

the difficulties that even trained healthcare providers encounter to confidently detect a pulse in an absent or low blood pressure state. [2]

INCIDENCE/ PREVALENCE

We found 24 observational studies (10 prospective, 14 retrospective) reporting the incidence of non-submersion out-of-hospital cardiorespiratory arrest in children (see table 1, p 15). [3] [4] [5] [6] [7] [8] [9] [10] [11] [12] [13] [14] [15] [16] [17] [18] [19] [20] [21] [22] [23] [24] [25] [26] Six studies reported the incidence in both adults and children, [8] [14] [19] [20] [21] [22] and 18 reported the incidence in children alone. [3] [4] [5] [6] [7] [9] [10] [11] [12] [13] [15] [16] [17] [18] [23] [24] [25] [26] The incidence in the general population in these studies ranged from 0.7 to 5.7/100,000 people per year. The incidence in children ranged from 3 to 18/100,000 children per year. Two prospective studies (761 children in total) found that 40% to 50% of cardiorespiratory arrests in children aged under 12 months occur out of hospital. [12] [17] Two prospective studies identified that children were aged under 18 months in approximately 50% (range 45%–65%) of out-of-hospital cardiorespiratory arrests. [12] [18]

AETIOLOGY/ RISK FACTORS

We found 37 observational studies reporting the causes of non-submersion pulseless arrests in a total of 3265 children. [4] [5] [6] [7] [8] [9] [10] [11] [12] [13] [15] [16] [18] [20] [21] [23] [24] [25] [26] [27] [28] [29] [30] [31] [32] [33] [34] [35] [36] [37] [38] [39] [40] [41] [42] [43] [44] The most common causes were undetermined (as in sudden infant death syndrome, 42%), trauma (19%), chronic disease (6%), and pneumonia (3%) (see table 2, p 16).

PROGNOSIS

We found no observational studies that investigated non-submersion arrests alone in a complete paediatric population. We found one systematic review (search date 2004) of 41 case series and cohort studies (9 prospective, 32 retrospective; total of 5363 children), which reported outcomes for out-of-hospital cardiopulmonary arrest of any cause, including submersion, in children up to 18 years. [45] Studies were excluded if survival, with survival-to-hospital discharge as a minimum, was not reported as an outcome. The overall survival rate (to hospital discharge) for the children meeting the paediatric Utstein style [1] definition for out-of-hospital non-submersion arrest was 5% (190/3475 children). Of the 190 surviving children, 43/190 (23%) had no or mild neurological disability, and 147/190 (77%) had moderate or severe neurological disability. Five subsequent prospective cohort studies of a total of 1503 children, including 90 children who sustained submersion events, reported a range of survival-to-hospital discharge between 0% and 6% (mean 4%). [17] [18] [20] [24] [26] Two subsequent retrospective cohort studies of a total of 234 children with non-submersion out-of-hospital cardiac arrest reported survival rates to hospital discharge between 3% and 5%, with 50% of the survivors sustaining severe neurological deficits. [23] [43] One subsequent retrospective cohort study of 193 children with out-of-hospital cardiac arrest, including 20 children who sustained submersion events, reported survival rates of 7%, with good neurological outcome in 80% of survivors. [25] One subsequent retrospective cohort study of 362 children with non-submersion, traumatic out-of-hospital cardiac arrest reported survival rates of 9%, with good neurological outcome in 3% who achieved sustained return of spontaneous circulation, and in 32% of those who survived to hospital discharge. [46] (See table 3., p 16) Two prospective cohort studies of a total of 23 paediatric patients who experienced out-of-hospital cardiac arrest during exertional activity reported survival rates of 64% to 67%. [21] [47] All members of this cohort had a primary cardiac aetiology for the sudden cardiac arrest and had an initial cardiac arrest rhythm that was shockable. [21] [47] We found one systematic review (search date 1997), which reported outcomes after cardiopulmonary resuscitation for both in-hospital and out-of-hospital arrests in children of any cause, including submersion. [48] Studies were excluded if they did not report on survival. The review found evidence from prospective and retrospective observational studies that out-of-hospital arrest of any cause in children has a poorer prognosis than within-hospital arrest (132/1568 [8%] children survived to hospital discharge after out-of-hospital arrest *v* 129/544 [24%] children after in-hospital arrests). About half of the survivors were involved in studies that reported neurological outcome. Of these, survival with "good neurological outcome" (i.e., normal or mild neurological deficit) was higher in children who arrested in hospital compared with those who arrested elsewhere (60/77 [78%] surviving children in hospital *v* 28/68 [41%] elsewhere). [48] (See also table 3., p 16) We identified one subsequent retrospective cohort study comparing outcomes of in-hospital and out-of-hospital cardiac arrests in children aged 24 hours to 18 years, which reported an out-of-hospital cardiac arrest survival of 53/138 (38%) and a rate of good neurological outcome of 31/138 (24%). [49] Another retrospective cohort study reporting on the long-term outcome of paediatric out-of-hospital cardiac arrest in 1683 paediatric patients treated for out-of-hospital cardiac arrest during the study period found that only 91 (5%) of these patients survived to hospital discharge, including 20 children who sustained submersion events. [50] Of those who survived to hospital discharge, survival at 1 year was 92%, 86% at 5 years, and 77% at 20 years. Long-term survivors more often had witnessed events, had presented with shockable rhythms, and had more favourable neurological outcomes at hospital discharge than patients who subsequently died.

AIMS OF INTERVENTION To improve survival and minimise neurological sequelae in children who suffer out-of-hospital cardiorespiratory arrest.

OUTCOMES **Mortality** out-of-hospital death rate; rate of death in hospital without return of spontaneous circulation; return of spontaneous circulation with subsequent death in hospital; **return of spontaneous circulation** with successful hospital discharge; **neurological outcomes** discharge from hospital with mild, moderate, severe, or no neurological sequelae; **adverse effects**.

METHODS **Search strategy** *BMJ Clinical Evidence* search and appraisal date November 2014. Databases used to identify studies for this systematic overview include: Medline 1966 to November 2014, Embase 1980 to November 2014, The Cochrane Database of Systematic Reviews 2014, issue 11 (1966 to date of issue), the Database of Abstracts of Reviews of Effects (DARE), and the Health Technology Assessment (HTA) database. **Inclusion criteria** Study design criteria for inclusion in this systematic overview were systematic reviews and RCTs published in English, at least single-blinded, and containing more than 20 individuals (10 in each arm), of whom more than 80% were followed up. There was no minimum length of follow-up. We excluded all studies described as 'open', 'open label', or not blinded unless blinding was impossible. *BMJ Clinical Evidence* does not necessarily report every study found (e.g., every systematic review). Rather, we report the most recent, relevant, and comprehensive studies identified through an agreed process involving our evidence team, editorial team, and expert contributors. **Evidence evaluation** A systematic literature search was conducted by our evidence team, who then assessed titles and abstracts, and finally selected articles for full text appraisal against inclusion and exclusion criteria agreed *a priori* with our expert contributors. In consultation with the expert contributors, studies were selected for inclusion and all data relevant to this overview extracted into the benefits and harms section of the review. In addition, information that did not meet our pre-defined criteria for inclusion in the benefits and harms section may have been reported in the 'Further information on studies' or 'Comment' sections (see below). **Adverse effects** All serious adverse effects, or those adverse effects reported as statistically significant, were included in the harms section of the overview. Pre-specified adverse effects identified as being clinically important were also reported, even if the results were not statistically significant. Although *BMJ Clinical Evidence* presents data on selected adverse effects reported in included studies, it is not meant to be, and cannot be, a comprehensive list of all adverse effects, contraindications, or interactions of included drugs or interventions. A reliable national or local drug database must be consulted for this information. **Comment and Clinical guide sections** In the Comment section of each intervention, our expert contributors may have provided additional comment and analysis of the evidence, which may include additional studies (over and above those identified via our systematic search) by way of background data or supporting information. As *BMJ Clinical Evidence* does not systematically search for studies reported in the Comment section, we cannot guarantee the completeness of the studies listed there or the robustness of methods. Our expert contributors add clinical context and interpretation to the Clinical guide sections where appropriate. **Structural changes this update** No changes. **Data and quality** To aid readability of the numerical data in our overviews, we round many percentages to the nearest whole number. Readers should be aware of this when relating percentages to summary statistics such as relative risks (RRs) and odds ratios (ORs). *BMJ Clinical Evidence* does not report all methodological details of included studies. Rather, it reports by exception any methodological issue or more general issue that may affect the weight a reader may put on an individual study, or the generalisability of the result. These issues may be reflected in the overall GRADE analysis. We have performed a GRADE evaluation of the quality of evidence for interventions included in this overview (see table, p 17). The categorisation of the quality of the evidence (into high, moderate, low, or very low) reflects the quality of evidence available for our chosen outcomes in our defined populations of interest. These categorisations are not necessarily a reflection of the overall methodological quality of any individual study, because the *BMJ Clinical Evidence* population and outcome of choice may represent only a small subset of the total outcomes reported, and population included, in any individual trial. For further details of how we perform the GRADE evaluation and the scoring system we use, please see our website (www.clinicalevidence.com).

QUESTION What are the effects of treatments for non-submersion out-of-hospital cardiorespiratory arrest in children?

OPTION AIRWAY MANAGEMENT AND VENTILATION

We found no direct information from RCTs about the use of airway management and ventilation, including bag-mask ventilation and intubation, in children who have arrested out of hospital.

For GRADE evaluation of interventions for cardiorespiratory arrest in children, see table, p 17 .

Benefits: We found no systematic review or RCTs on the effects of airway management and ventilation in children who have suffered out-of-hospital cardiorespiratory arrest.

Harms: We found no RCTs.

Comment: It is widely accepted, based on indirect evidence and extrapolation from adult data, that rapid establishment of an airway and effective management of ventilation should be undertaken in a child who has arrested, and it would be considered unethical to test its role in a placebo-controlled trial.

Clinical guide
There is general consensus that rapid establishment of an airway and effective management of ventilation are crucial initial interventions in the management of a paediatric out-of-hospital cardiopulmonary arrest.

OPTION BYSTANDER CARDIOPULMONARY RESUSCITATION

We found no direct information from RCTs about the use of bystander cardiopulmonary resuscitation in children who have experienced a cardiac arrest out of hospital.

Note
Cardiopulmonary resuscitation, including compressions, ventilations, or both, is an important intervention in out-of-hospital cardiopulmonary arrest.

For GRADE evaluation of interventions for cardiorespiratory arrest in children, **see table, p 17 .**

Benefits: We found no systematic reviews or RCTs on the effects of bystander cardiopulmonary resuscitation in children who have suffered out-of-hospital cardiorespiratory arrest.

Harms: We found no studies.

Comment: Placebo-controlled trials would be considered unethical.

We found one systematic review (search date 2004, 5363 children who had arrested outside hospital, including submersion cases) of prospective and retrospective observational studies, [45] and two subsequent observational studies (709 children in total). [18] [43] The review included nine studies that quantified bystander cardiopulmonary resuscitation data, of which seven reported on survival to hospital discharge (41/433 [9%] with bystander cardiopulmonary resuscitation *v* 49/1042 [5%] with no bystander cardiopulmonary resuscitation; significance not assessed because of heterogeneity). Risk ratios for survival to hospital discharge varied widely (0.53 to 4.7), and the review found significant heterogeneity among studies (P = 0.001). One study had no survivors and was excluded from pooled analysis. The review concluded that pooled analysis of the six remaining studies failed to demonstrate a consistent association between bystander cardiopulmonary resuscitation and survival (data presented graphically in the review). Cardiopulmonary resuscitation was not randomly allocated, and children resuscitated may have been systematically different from those who did not receive resuscitation. The apparent survival rates for witnessed arrests and arrests with bystander-initiated cardiopulmonary resuscitation may be artificially high because of inappropriate evaluation of true arrest. However, assuming that confounding variables were evenly distributed between groups, the best estimate of the benefit of cardiopulmonary resuscitation is a 30% absolute increase in the probability that children will be discharged alive from hospital.

The first subsequent observational study (85 children) found that bystander cardiopulmonary resuscitation was significantly associated with increased survival compared with no bystander cardiopulmonary resuscitation (survival to hospital discharge: 3/20 [15%] with bystander cardiopulmonary resuscitation *v* 1/65 [2%] without bystander cardiopulmonary resuscitation; P = 0.04). [43] The second prospective observational study (624 people aged <20 years, 29 of whom suffered submersion arrests) reported bystander cardiopulmonary resuscitation initiation in 217/624 (35%) of paediatric out-of-hospital cardiac arrests. [18] The study found no significant difference in rates of survival with initiation of bystander cardiopulmonary resuscitation (no data reported), although the study was under-powered to detect a relationship because of low numbers of survivors (40/624 [6%]). [18]

We also found one population-based cohort study (7624 children aged <19 years, including 5323 with non-cardiac origin), which reported that children who received bystander cardiopulmonary resuscitation had increased odds of 1-month survival (OR 2.81, 95% CI 2.30 to 3.44) and increased odds of favourable neurological outcome (OR 4.55, 95% CI 3.35 to 6.18) compared with children who did not receive bystander cardiopulmonary resuscitation. [51]

Two population-based cohort studies examined the impact of dispatcher instruction on bystander cardiopulmonary resuscitation. The first study, a retrospective review of paediatric out-of-hospital cardiac arrests (1780 people aged <20 years), found that telephone instruction regarding bystander cardiopulmonary resuscitation was associated with a significantly higher proportion of patients receiving chest compressions (69% *v* 28%; P <0.001), improvements in 1-month survival (19% *v* 11%; P <0.001), and a trend towards an increase in favourable neurological outcomes (7% *v* 5%; P = 0.068). [52] The second, a prospective study of paediatric out-of-hospital cardiac arrests (5009 people aged <18 years), examined three groups of patients: those who received bystander cardiopulmonary resuscitation with dispatcher instruction (2019 children), those who received bystander cardiopulmonary resuscitation without dispatcher instruction (703 children), and those who did not receive bystander cardiopulmonary resuscitation (2287 children). The study reported increased odds of 1-month survival in patients who received bystander cardiopulmonary resuscitation with dispatcher instruction (adjusted OR 1.63, 95% CI 1.32 to 2.02) or bystander cardiopulmonary resuscitation without dispatcher instruction (adjusted OR 1.62, 95% CI 1.23 to 2.11) compared with patients who did not receive bystander cardiopulmonary resuscitation. The study also reported increased odds of favourable neurological outcome in patients who received bystander cardiopulmonary resuscitation with dispatcher instruction (adjusted OR 1.81, 95% CI 1.24 to 2.67) or bystander cardiopulmonary resuscitation without dispatcher instruction (adjusted OR 1.68, 95% CI 1.07 to 2.62). [53] Neither of the studies indicated whether or not the population of study included submersion cases.

Potential harms include injury resulting from unnecessary chest compression after respiratory arrest with intact circulation. The systematic review [45] and the observational studies [18] [43] gave no information about adverse effects.

Clinical guide
It is widely accepted that cardiopulmonary resuscitation, including compressions, ventilations, or both, should be undertaken in children who have arrested, although the evidence remains weak. On the basis of observational evidence and experience, most clinicians regard bystander cardiopulmonary resuscitation to be an important intervention in out-of-hospital cardiopulmonary arrest. The 2015 International Liaison Committee on Resuscitation's Consensus on science with treatment recommendations encourages trained rescuers to provide both ventilations and chest compressions, recognising initiation of timely rescue breathing as part of effective cardiopulmonary resuscitation in children, and lessening the emphasis (in the 2010 statement) on compression initiation even before airway or breathing management has begun. The consensus recommendation continues to encourage those rescuers who are reluctant or unable to perform ventilations to institute and continue chest compressions without interruption. [54] Trained rescuers are advised to apply a 'push hard, push fast' technique for chest compressions, allowing for optimal maintenance of circulation while allowing full chest recoil. Full chest recoil and strict attention to ventilation technique may minimise the negative effect of excessive positive intrathoracic pressure on cardiac output. [2]

OPTION TRAINING PARENTS TO PERFORM CARDIOPULMONARY RESUSCITATION

We found no direct information from RCTs about the effects of training parents to perform cardiopulmonary resuscitation in children who have arrested in the community.

For GRADE evaluation of interventions for cardiorespiratory arrest in children, see table, p 17 .

Benefits: **Training parents to perform cardiopulmonary resuscitation:**
We found no systematic review or RCTs on the effects of training parents to perform cardiopulmonary resuscitation in children who have arrested in the community.

Harms: Potential harms include injury resulting from unnecessary chest compression after respiratory arrest with intact circulation. The systematic review [45] and the observational studies [18] [43] discussed in the option on bystander cardiopulmonary resuscitation gave no information about adverse effects.

Comment: Placebo-controlled trials would be considered unethical.

Clinical guide
It is widely accepted that cardiopulmonary resuscitation, including compressions, ventilations, or both, should be undertaken in children who have arrested, although the evidence remains weak. On the basis of observational evidence and experience, most clinicians regard bystander cardiopulmonary resuscitation to be an important intervention in out-of-hospital cardiopulmonary arrest, although the effects of training parents in cardiopulmonary resuscitation are unknown.

OPTION DIRECT CURRENT CARDIAC SHOCK

We found no direct information from RCTs about the use of direct current cardiac shock in children who have arrested from ventricular fibrillation or pulseless ventricular tachycardia out of hospital.

For GRADE evaluation of interventions for cardiorespiratory arrest in children, see table, p 17 .

Benefits: We found no systematic review or RCTs on the use of direct current cardiac shock in children who have arrested out of hospital.

Harms: We found no studies.

Comment: Placebo-controlled trials would be considered unethical.

In children with ventricular fibrillation or pulseless ventricular tachycardia

The studies reported in this section do not fulfil the exact inclusion criteria for this overview; however, the children included do fit into our population of interest because both these rhythms result in a cessation of 'useful' cardiac mechanical activity (it is disordered such that the state rendered is one of pulselessness and apnoea — that is, the resultant clinical state is one of cardiorespiratory arrest).

A population-based observational study (7624 children aged <19 years, including 5323 with non-cardiac origin) reported an initial rhythm of ventricular fibrillation (VF) or pulseless ventricular tachycardia (PVT) in 412 (5%) children. In this study, children who received a shock via an automated external defibrillator (AED) had increased odds of 1-month survival (OR 3.51, 95% CI 1.81 to 6.81) and increased odds of favourable neurological outcome (OR 5.13, 95% CI 2.64 to 9.96). Children who were defibrillated by the emergency medical service also had increased odds of 1-month survival (OR 4.01, 95% CI 3.03 to 5.32) and increased odds of favourable neurological outcome (OR 3.26, 95% CI 2.30 to 4.62). [51]

One prospective cohort study (624 children aged <20 years, including 29 children with submersion) reported an initial rhythm of VF or PVT in 35 (6%) children, of whom 7 (20%) survived to hospital discharge. Children whose initial rhythm was VF or PVT were statistically more likely to survive to hospital discharge (survival between children with VF/PVT rhythms compared with asystole or pulseless electrical activity: OR: 4.78, 95% CI 1.85 to 12.33; P = 0.0012). [18]

One secondary analysis of a prospective observational study of 217 children who experienced out-of-hospital arrest of presumed cardiac origin reported use of an AED in 39 patients (21 children aged 1–8 years, 18 children aged 9–17 years). An initial rhythm that was shockable was documented in 43 children (15 children aged 1–8 years, 28 children aged 9–17 years). Return of spontaneous circulation (ROSC) occurred in 13 children aged 1 to 8 years and 25 children aged 9 to 17 years. Two children aged 1 to 8 years and 14 children aged 9 to 17 years survived to hospital discharge, with a good neurological outcome in two and nine of the children, respectively. This study reported no effect of AED use on the prevalence of survival in either group, possibly due to the low survival rates. [55]

One secondary analysis of a prospective observational study of 241 children who experienced in-hospital and out-of-hospital arrest, including submersion as a diagnosis, reported VF or PVT as the first documented rhythm in 19 children (10 in hospital, 9 out of hospital), and progression to VF or PVT in 25 children (12 in hospital, 13 out of hospital). [56] Three of 44 children who received at least one electric shock (one out-of-hospital arrest) survived at 1 year. Children who had a defibrillation attempt within the first 4 minutes were more likely to achieve ROSC, initial survival, and final survival than those shocked later, although statistical significance was achieved only for initial survival (P = 0.03). Those children in whom the initial documented rhythm was VF or PVT were significantly more likely to experience ROSC (P = 0.025), initial survival (P = 0.005), and final survival (P = 0.073). Children who were treated with an initial shock dose of 2 J/kg or less were more likely to require more than one shock than those treated with an initial dose higher than 2 J/kg, but there were no survival differences between these groups. [56]

One prospective observational study of cardiac arrest in 14 high school athletes treated with AEDs reported that 13 of 14 students received a shock via the AED, suggesting an initial rhythm of either VF or ventricular tachycardia (VT). Nine of 13 (69%) athletes who were shocked survived to hospital discharge. Mean time from arrest to initial cardiopulmonary resuscitation was 1.5 minutes (range 0–5.75 minutes) and mean time from arrest to initial shock deployment was 3.6 minutes (range 0.75–11.5 minutes). No other statistical data were provided, but the study is noteworthy for the reported high survival rate in those athletes who were treated with shock via the AED. [21]

One retrospective study (29 children with VF who had arrested out of hospital from a variety of causes, including submersion) found that, of 27 children who were defibrillated, 11 survived (5 with no sequelae, 6 with severe disability). The five children with good outcome all received defibrillation within 10 minutes of arrest (time to defibrillation not given for those who died). Data on the two children who were not defibrillated were not presented. [57] One retrospective study (13 children with VF who arrested out of hospital, including one submersion-related arrest) found that, of 13 children given an initial shock (2 J/kg as initial dose) within a median time from arrest of 11 minutes, defibrillated a total of 14 times, none survived to hospital discharge. [58]

In children with asystole

A secondary analysis of data from a prospective study (241 children, 4 children with submersion injury) that compared in-hospital and out-of-hospital paediatric cardiopulmonary arrest identified 44/241 (18%) children who received at least one electric shock. In 25 children (12 in hospital and 13 out of hospital), the initial rhythm was non-shockable, but VF or PVT developed during cardiopulmonary resuscitation attempts. [56] The study reported that ROSC was achieved in 12/25 (48%), 6/25 (24%) survived initially, but none survived to 1 year. The study found that in these children, rates of ROSC (P = 0.025), initial survival (P = 0.005), and final survival (P = 0.073) were significantly lower than for those children in whom the initial rhythm was shockable. [56]

One retrospective study in 90 children with asystole (including those who had arrested after submersion) found that 49 (54%) had received direct current cardiac shock treatment. None of the children survived to hospital discharge, regardless of whether direct current cardiac shock was given. [59] We found one systematic review of observational studies that recorded electrocardiogram rhythm (search date 1997, 1420 children who had arrested outside hospital). [48] Bradyasystole or pulseless electrical activity was found in 73%, whereas VF or PVT was found in 10%. The review found that survival after VF or VT arrest was higher than after asystolic arrest in children. Survival to discharge reported in the systematic review was 39/802 (5%) for children with initial rhythm asystole and 29/97 (30%) with initial rhythm ventricular fibrillation or VT.

Clinical guide

Although the evidence for benefit from direct current cardiac shock is weak, there is widespread consensus that children who arrest outside hospital and are found to have VF or PVT should receive direct current cardiac shock treatment. There are consensus recommendations from the American College of Cardiology Evidence-Based Practice Guidelines (2008), which recommend implantable cardioverter-defibrillator (ICD) implantation in paediatric survivors of cardiac arrest after evaluation, to define the cause of the event and to exclude any reversible causes, in 20 references pertinent to the paediatric population (Class 1 Recommendation, Level of Evidence B). [60]

OPTION STANDARD DOSE INTRAVENOUS ADRENALINE (EPINEPHRINE)

We found no direct information from RCTs about whether intravenous adrenaline at standard dose is better than no active treatment in establishing return of spontaneous circulation in children who have arrested out of hospital.

For GRADE evaluation of interventions for cardiorespiratory arrest in children, see table, p 17 .

Benefits:

Intravenous adrenaline versus placebo:

We found no RCTs in children who have arrested in the community comparing adrenaline with placebo.

Standard dose versus high dose intravenous adrenaline:

See Benefits of High-dose intravenous adrenaline, p 9 .

Harms:

We found no RCTs.

Comment:

Intravenous adrenaline (epinephrine) at 'standard dose' (0.01 mg/kg) is a widely accepted treatment for establishing return of spontaneous circulation in children who have arrested out of hospital.

We found one systematic review (search date 2013), which identified 14 RCTs evaluating the use of standard dose adrenaline in the treatment of adults with out-of-hospital cardiopulmonary arrest. [61] Only one RCT (double-blinded) compared standard dose (1 mg) adrenaline to placebo administered intravenously to 601 adult patients in the pre-hospital setting. [62] Analysis was by intention to treat. Subgroup analysis in patients with shockable (46%) or non-shockable (54%) initial rhythm found no significant difference between standard dose adrenaline and placebo in survival to hospital discharge, despite a significantly higher likelihood of return of spontaneous circulation. [62] A large, double-blinded, placebo-controlled trial in adult patients with out-of-hospital cardiopulmonary arrest is underway. [63] It may be challenging to generalise any results from this trial to children, given

the different pathophysiology and aetiologies of cardiac arrest in adults compared with children, However, a placebo-controlled trial in children may be considered, depending on the results from this adult trial.

High dose versus low dose adrenaline
We found one systematic review (search date 2011), which identified one RCT evaluating the use of adrenaline in the treatment of people, including children, in cardiorespiratory arrest. [64]

Clinical guide
Despite a lack of direct evidence for its benefit, there is consensus that standard dose (0.01 mg/kg) adrenaline is the first medication to be used for the management of out-of-hospital cardiopulmonary arrest in children. Although many clinicians have in the past used high dose (0.1 mg/kg) adrenaline for second and subsequent doses, there is no satisfactory evidence of any benefit in improving survival and weak evidence for a trend towards worse neurological outcomes with its use. Further RCTs would be feasible but would need to be undertaken in larger numbers of children, with consistent outcomes measured in accordance with Utstein guidelines.

OPTION HIGH DOSE INTRAVENOUS ADRENALINE AT HIGH DOSE (COMPARED WITH STANDARD DOSE)

Mortality
High dose adrenaline compared with standard dose adrenaline We don't know how high dose adrenaline and standard dose adrenaline compare at increasing survival rates to hospital discharge in children who have experienced out-of-hospital cardiac arrest (very low-quality evidence).

Return of spontaneous circulation
High dose adrenaline compared with standard dose adrenaline We don't know how high dose adrenaline and standard dose adrenaline compare at improving return to spontaneous circulation in children who have experienced out-of-hospital cardiac arrest (very low-quality evidence).

Neurological outcomes
High dose adrenaline compared with standard dose adrenaline We don't know how high dose adrenaline and standard dose adrenaline compare at improving neurological outcomes in children who have experienced out-of-hospital cardiac arrest (very low-quality evidence).

Note
We found no direct information from RCTs about whether intravenous adrenaline is better than no active treatment in establishing spontaneous circulation in children who have experienced cardiac arrest out of hospital.

For GRADE evaluation of interventions for cardiorespiratory arrest in children, see table, p 17 .

Benefits:

High dose versus standard dose intravenous adrenaline:
We found one systematic review (search date 2011), which identified one RCT evaluating the use of adrenaline in the treatment of people, including children, in cardiorespiratory arrest. [64] The RCT (multi-centre, non-blinded) included 213 people aged up to 22 years (mean age 33.7 months) with out-of-hospital cardiopulmonary arrest from various causes, including submersion). [65] The RCT compared high dose (0.1 mg/kg for the first dose; 0.2 mg/kg for subsequent doses) with standard dose (0.01 mg/kg for the first dose; 0.02 mg/kg for subsequent doses) adrenaline administered intravenously, intraosseously, or endotracheally; all doses administered via the endotracheal route were doubled. [65] Analysis was by intention to treat. Subgroup analysis in people with either medical (72%) or traumatic (28%) aetiology of arrest found no significant difference between high dose and standard dose adrenaline in return of spontaneous circulation, survival to 24 hours, or survival to hospital discharge. [65] Subgroup analysis, excluding children with sudden infant death syndrome, found no significant difference in outcomes between high and standard doses. [65] However, caution should be used when interpreting these results because of methodological limitations of the RCT. It was not adequately powered to demonstrate any significant effect convincingly, because it was stopped after a change in waiver of informed consent legislation before it achieved the calculated sample size of 240. There was possible enrolment bias towards high dose adrenaline, because the study protocol was modified after revision of the paediatric advanced life support guidelines, allowing for higher doses of adrenaline to be used in people requiring multiple doses. The randomisation method was not consistent across all centres, although a biased randomisation process could not be demonstrated.

Harms:

The RCT [65] gave no information about adverse effects of treatment.

Comment:

High dose versus low dose adrenaline

We found one prospective cohort study (283 children, containing subgroup analysis of 87 children given at least one dose of adrenaline: 11 children given 0.01 mg/kg; 76 children given 0.01 mg/kg for the first dose and 0.1 mg/kg for subsequent doses) that reported no significant difference between the high dose and standard dose groups in return of spontaneous circulation, survival to hospital discharge, or survival at 1 year. [66] Mean age and weight at baseline were significantly higher in the standard dose group than in the high dose group (mean age: 97.1 months with standard dose *v* 29.9 months with high dose; P = 0.03; mean weight: 24.7 kg with standard dose *v* 11.9 kg with high dose; P = 0.037).

We also found two small retrospective observational studies (128 children), which found no significant difference in rates of survival to hospital discharge between low or single dose and high or multiple dose adrenaline, although these studies may have been too small to detect a significant difference. [9] [11] In all, one RCT and three small observational studies (1 prospective, 2 retrospective) found no evidence of a difference in return of spontaneous circulation, survival to hospital discharge, or neurological outcome between standard dose and high dose adrenaline, although the study sample sizes were all too small to detect a significant difference. [9] [11] [65] On the basis of two in-hospital [67] [68] and two out-of-hospital [65] [9] paediatric studies demonstrating no improvement in survival rates and trends towards worse neurological outcome for the high dose adrenaline group, the 2010 International Liaison Committee consensus statement recommended against routine use of high dose adrenaline. [69] The 2015 ILCOR statement states only that it is reasonable to use standard dose adrenaline. [54]

Clinical guide

Despite a lack of direct evidence for its benefit, there is consensus that standard dose (0.01 mg/kg) adrenaline is the first medication to be used for the management of out-of-hospital cardiopulmonary arrest in children. Although many clinicians have in the past used high dose (0.1 mg/kg) adrenaline for second and subsequent doses, there is no satisfactory evidence of any benefit in improving survival and weak evidence for a trend towards worse neurological outcomes with its use. Further RCTs would be feasible, but would need to be undertaken in larger numbers of children, with consistent outcomes measured in accordance with Utstein guidelines.

OPTION INTRAVENOUS SODIUM BICARBONATE

We found no direct information from RCTs about the effects of intravenous sodium bicarbonate in children who have arrested in the community.

For GRADE evaluation of interventions for cardiorespiratory arrest in children, see table, p 17 .

Benefits: We found no systematic review or RCTs of sufficient quality.

Harms: We found no studies.

Comment: Sodium bicarbonate is widely believed to be effective in arrest associated with hyperkalaemic ventricular tachycardia or fibrillation, but we found no prospective evidence supporting this.

OPTION INTUBATION VERSUS BAG-MASK VENTILATION

We found no direct information from RCTs about the effects of intubation compared with bag-mask ventilation in children who have experienced cardiac arrest in the community.

Note

It is essential to establish a rapid airway and effectively manage ventilation by whatever method is appropriate or feasible in each individual circumstance.

For GRADE evaluation of interventions for cardiorespiratory arrest in children, see table, p 17 .

Benefits: We found one systematic review (search date 2007, 3 trials) of out-of-hospital emergency intubation. [70] Two of the trials identified by the review included adult populations only and, therefore, will not be reported further here. The third study identified by the review was a non-randomised control trial, which, as such, does not meet *BMJ Clinical Evidence* inclusion criteria. The results of the trial are discussed in the Comment section.

Harms: We found no studies.

Comment: The non-randomised study (830 children aged 12 years or younger requiring airway management in the community, including 589 [71%] children who had non-traumatic out-of-hospital cardiac arrest,

98 [12%] of whom suffered arrest after submersion) compared bag-mask ventilation (with endotracheal intubation performed later by an emergency department physician) with endotracheal intubation by paramedic staff trained in both techniques. Outcome measures included primary outcomes of mortality and degree of disability at discharge from hospital. [71] The trial found no significant difference in rates of survival or good neurological outcome (normal, mild deficit, or no change from baseline function) between the two treatment groups (survival: 123/404 [30%] with bag-mask ventilation *v* 110/416 [26%] with intubation; OR 0.82, 95% CI 0.61 to 1.11; good neurological outcome: 92/404 [23%] with bag-mask ventilation *v* 85/416 [20%] with intubation; OR 0.87, 95% CI 0.62 to 1.22). [71] The trial did not report on the frequency of cardiorespiratory arrest compared with that of respiratory arrest. Analysis was by intention to treat. Intubation and bag-mask ventilation were not mutually exclusive in the trial. The trial protocol allowed bag-mask ventilation before intubation and after unsuccessful intubation. Of children allocated to intubation, 115/420 (27%) received bag-mask ventilation before intubation, 128/420 (30%) received bag-mask ventilation after attempted intubation, 4/420 (1%) were lost to follow-up, and the remaining 177/420 (42%) received intubation that was believed to be successful. Of 410 children allocated to bag-mask ventilation, 10 (2%) children were intubated successfully (although in violation of study protocol), 9 (2%) received bag-mask ventilation after attempted intubation, 6 (1.5%) were lost to follow-up, and the remainder received bag-mask ventilation in accordance with study protocol. [71]

The paediatric trial identified by the review [70] found that the time spent at the scene of the arrest was longer when intubation was intended, and this was the only significant determinant of a longer total time from dispatch of paramedic team to arrival at hospital (mean time at scene: 9 minutes with bag-mask *v* 11 minutes with intubation; P <0.001; mean total time: 20 minutes with bag-mask *v* 23 minutes with intubation; P <0.001). [71] However, it found no significant difference between bag-mask ventilation and intubation in complications (complications in 727 children for whom data were available: gastric distension: 31% with bag-mask *v* 7% with intubation; P = 0.20; vomiting: 14% with bag-mask *v* 14% with intubation; P = 0.82; aspiration: 14% with bag-mask *v* 15% with intubation; P = 0.84; oral or airway trauma: 1% with bag-mask *v* 2% with intubation; P = 0.24). A total of 186 children across both treatment groups were considered by paramedic staff to be successfully intubated. Of these, oesophageal intubation occurred in three children (2%); the tube became dislodged in 27 children (14%; unrecognised in 12 children, recognised in 15); right main bronchus intubation occurred in 33 children (18%); and an incorrect size of tube was used in 44 children (24%). Death occurred in all but one of the children with oesophageal intubation or unrecognised dislodging of the tube. [70] [71]

The authors of the systematic review concluded that there is no sufficient evidence base to extend the practice of pre-hospital intubation in urban systems. [70]

Clinical guide

In choosing between bag-mask ventilation and intubation, different factors need to be considered, such as the skill set of the emergency medical personnel attending the scene, distance and time away from the closest hospital with paediatric expertise, and the mode of transport to hospital. Healthcare professionals with little experience of intubation may be reassured to know that we found no evidence to suggest that intubation was better than bag-mask ventilation for improving survival or neurological outcomes following cardiorespiratory arrest in the community. The most important factors are the rapid establishment of an airway and effective management of ventilation, by whatever method is most appropriate or feasible in each individual circumstance.

OPTION TARGETED TEMPERATURE MANAGEMENT AFTER OUT-OF-HOSPITAL ARREST

We found no direct information from RCTs about the effects of targeted temperature management (induced hypothermia or therapeutic normothermia) after out-of-hospital cardiac arrest in children.

For GRADE evaluation of interventions for cardiorespiratory arrest in children, see table, p 17 .

Benefits: We found two systematic reviews (search dates 2011; [72] and 2011 [73]), neither of which found any RCTs assessing the effects of targeted temperature management (induced hypothermia or therapeutic normothermia) on out-of-hospital cardiac arrest in children.

Harms: We found no studies.

Comment: Animal models of cardiac arrest have indicated that hypothermia may be beneficial to the injured brain. [74] [75] [76] Two RCTs of induced hypothermia (temperature 32–34°C) in a highly selected population of adults following out-of-hospital cardiac arrest due to ventricular fibrillation found increased survival and good neurological outcomes. [77] [78] The rates of sepsis, pneumonia, bleeding, arrhythmias, and hyperglycaemia were higher in adults receiving hypothermia, but these differences were not significant. Lower heart rates and increased systemic vascular resistance

were also identified in the hypothermia groups, but these differences were also not significant. Subsequently, one large international multicentre RCT of targeted temperature management in 950 adults after out-of-hospital cardiac arrest found no difference in survival or survival with good neurological outcomes. [79]

RCT published after search date

Prior to publication of this update, but after our search date, one study published the results of a large, multi-centre randomised controlled trial comparing two targeted temperature interventions (therapeutic hypothermia at a target temperature of 33.0°C *v* therapeutic normothermia at a target temperature of 36.8°C) in children who remained unconscious after out-of-hospital cardiac arrest. [80] A total of 275 patients admitted to 38 children's hospitals were randomised within 6 hours of return of spontaneous circulation and treated for 120 hours. The results indicated no significant differences in survival with good neurobehavioural outcome at 12 months' follow-up (20% with therapeutic hypothermia *v* 12% with normothermia; P = 0.14). The authors concluded that therapeutic hypothermia does not confer any benefit in survival with good functional outcome in children who remain comatose after out-of-hospital cardiac arrest. However, it is important to note that active temperature management was necessary in both groups.

Clinical guide

There is still some uncertainty about the use of induced hypothermia in children who have arrested out of hospital. [2] [69] Although there is no strong evidence to support the use of induced hypothermia to below normal body temperature in children with out-of-hospital cardiopulmonary arrest, avoidance of hyperthermia is likely beneficial and targeted temperature management to achieve normothermia is recommended. [80]

GLOSSARY

Asystole The absence of cardiac electrical activity.

Bradyasystole Bradycardia clinically indistinguishable from asystole.

Initial rhythm asystole The absence of cardiac electrical activity at initial determination.

Initial rhythm ventricular fibrillation Electrical rhythm is ventricular fibrillation at initial determination.

Pulseless arrest Absence of palpable pulse, following cardiorespiratory arrest.

Pulseless electrical activity The presence of cardiac electrical activity in the absence of a palpable pulse.

Pulseless ventricular tachycardia Electrical rhythm of ventricular tachycardia in the absence of a palpable pulse.

Respiratory arrest Absence of respiratory activity.

Sudden infant death syndrome The sudden unexpected death of a child, usually between the ages of 1 month and 1 year, for which a thorough postmortem examination does not define an adequate cause of death. Near miss sudden infant death syndrome refers to survival of a child after an unexpected arrest of unknown cause.

Paediatric Utstein style Uniform guidelines for reporting paediatric resuscitation data, based on recommended guidelines for adult out-of-hospital cardiac arrest developed at the Utstein conference in 1991. [1]

Very low-quality evidence Any estimate of effect is very uncertain.

SUBSTANTIVE CHANGES

High dose intravenous adrenaline (compared with standard dose) One systematic review added. [64] Categorisation unchanged (unknown effectiveness).

Targeted temperature management after out-of-hospital arrest Two systematic reviews added. [72] [73] One RCT in adults [79] and one RCT published after the search date of this review [80] were added to Comment section. Categorisation unchanged (unknown effectiveness).

Bystander cardiopulmonary resuscitation Three studies were added to the Comment section. [51] [52] [53] Evidence re-evaluated. Categorisation unchanged (likely to be beneficial).

Direct current cardiac shock Three studies were added to the Comment section. [51] [55] [56] Evidence re-evaluated. Categorisation unchanged (likely to be beneficial).

Standard dose intravenous adrenaline (epinephrine) One systematic review added to the Comment section. [64] Evidence re-evaluated. Categorisation unchanged (likely to be beneficial).

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Competing interests: KK and HW declare that they have no competing interests.
The authors would like to acknowledge the previous contributor to this overview, David Creery.

Disclaimer

TABLE 1 **Incidence of non-submersion out-of-hospital cardiorespiratory arrest in children* (see text).**

Ref	Location	Year	Patient population	Incidence/100,000 people in total population	Incidence/100,000 children
[13]	Manitoba, CA	1982	Children (1 mo to 16 y)	2.9	ND
[4]	King County, US	1983	Children (<18 y)	2.4	9.9
[5]	Jerusalem, Israel	1986	Children (14 y or under)	2.5	6.9
[6]	Fresno, US	1987	Children (<19 y)	5.7	ND
[7]	Midwestern US	1990	Children (<18 y)	4.7	ND
[8]	King County, US	1992	Adults and children	2.4	10.1
[14]	Taipei, TW	1994	Adults and children	1.3	ND
[9]	San Francisco, US	1995	Children (<18 y)	2.2	16.1
[10]	Helsinki, FI	1995	Children (<16 y)	1.4	9.1
[11]	Birmingham, US	1995	Children (13 y or under)	ND	6.9
[44]	Leicester, UK	1997	Children (16 y or under)	1.39	6.4
[12]	Houston, US	1999	Children (17 y or under)	4.9	18
[3]	Southern Israel	2000	Children (12 y or under)	3.5	7.8
[15]	California, US	2004	Children (<12 y, or 40 kg or under)	1.58	6.3
[17]	Ontario, CA	2002	Children (<19 y)	1.7	8.4
[18]	US, Canada	2006	Children (<20 y)	2.5	8.04†
[19]	Washington, US	1990–2005	Children in school age 3–18 y and adults on the school premises	0.03	0.18/100,000 student school years‡
[20]	Queretaro, MX	2006–2007	Adults and children age 1–15 y	0.81	ND‡
[21]	US	2007	High school children and adults on the premises	ND	4.4/1,000,000 high school students
[25]	Melbourne, AU	2010	Children age 0–16 y	0.72	3
[24]	North Holland, NL	2011	Children age 0–20 y	2.43	9
[26]	New York City, US	2012	Children (<18 y)	1.8	7.6
[23]	Taiwan	2013	Children (<19 y)	ND	ND
[22]	Perth, Western Australia	2014	Adults and children age 1–15 y	6.5	ND

*Incidence represents arrests per 100,000 population per year. †Did not include traumatic cases, submersion as a cause was included in the number for the incidence per 100,000 children. ‡Different data because of different populations.
mo, months; ND, no data; y, years.

TABLE 2 **Causes of non-submersion out-of-hospital cardiorespiratory arrest in children* (see text).**

Cause	Number of arrests (%)
Undetermined	1357 (41.6)
Trauma	634 (19.4)
Chronic disease	201 (6.1)
Pneumonia	130 (3.4)
Overdose	48 (1.5)
Aspiration	26 (0.80)
Non-accidental injury	24 (0.73)
Other	845 (25.9)
Total	3265 (100)

*Figures represent the numbers of arrests in children with each diagnosis.

TABLE 3 **Prognosis for out-of-hospital cardiorespiratory arrest.**

Ref	Population	ROSC	Survival to hospital discharge	Survival without neurological sequelae
[17]	Children <19 y	25/503 (5%)	9/503 (2%)	NR
[45]	Children <18 y	406/1813 (22%)	190/3475 (5%)	43/2198 (2%)
[43]	Children <17 y	26/84 (31%)	4/84 (5%)	2/84 (2%)
[48]	Age <20 y	NR	94/1423 (7%)	13/1423 (1%)
[18]	Age <20 y	65/121 (10%)*	40/621 (6%)*	NR
[24]	Children age 0–20 y	51/223(22.9%)	12/223 (5.4%)	10/223 (4.5%)
[23]	Children (<19 y)	51/150 (34%)	4/150 (2.7%)	NR
[25]	Children age 0–16 y	49/193 (25.4%)	15/193 (7.8%)	15/193 (7.8%)
[26]	Children (<18 y)	NR	6/147 (4.1%)	NR
[46]	Children (<19 y)	152/362 (42%)	34/362 (9.4%)	11/362 (3%)

*This reference specified ROSC in the field.
NR, not reported; ROSC, return of spontaneous circulation; y, years.

TABLE **GRADE evaluation of interventions for cardiopulmonary arrest in children (out of hospital).**

Important outcomes	Death, return of spontaneous circulation, neurological outcomes, adverse effects								
Number of studies (participants)	**Outcome**	**Comparison**	**Type of evidence**	**Quality**	**Consistency**	**Directness**	**Effect size**	**GRADE**	**Comment**
What are the effects of treatments for non-submersion out-of-hospital cardiorespiratory arrest in children?									
1 (213) [65]	Mortality	High dose adrenaline *v* standard dose adrenaline	4	–3	0	–1	0	Very low	Quality points deducted for methodological, randomisation, and blinding flaws; directness point deducted for various routes of administration
1 (213) [65]	Return of spontaneous circulation	High dose adrenaline *v* standard dose adrenaline	4	–3	0	–1	0	Very low	Quality points deducted for methodological, randomisation, and blinding flaws; directness point deducted for various routes of administration
1 (213) [65]	Neurological outcomes	High dose adrenaline *v* standard dose adrenaline	4	–3	0	–1	0	Very low	Quality points deducted for low number of events and methodological, randomisation, and blinding flaws; directness point deducted for various routes of administration

Type of evidence: 4 = RCT; 2 = Observational; 1 = Non-analytical/expert opinion.
Consistency: similarity of results across studies.
Directness: generalisability of population or outcomes.
Effect size: based on relative risk or odds ratio.